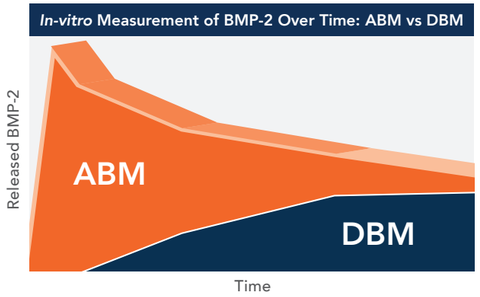
Evaluation of Osteoinductive Potential

An *in-vitro* study was conducted to examine accessibility to bioactive proteins in ABM and DBM.[1] The content of BMP-2, which has been shown to be strongly correlated with osteoinductive potential *in vivo*[3], was measured over time using an Enzyme Linked Immunosorbent Assay (ELISA). The results are shown graphically below.



Study Results

- Soluble BMP-2 was detected in ABM at an earlier time compared to particulate DBM.
- ABM's open pore structure provides earlier accessibility to bone proteins.
- DBM provides accessibility to bone proteins at later time points.

Indications for Use

OsteoSurge® 100 is intended for filling voids and gaps in the skeletal system that are not intrinsic to the stability of the bony structure. OsteoSurge 100 is indicated for use as a bone graft extender in the spine, extremities and pelvis or as a bone void filler in the extremities and pelvis. The voids or gaps may be surgically created defects or the result of traumatic injury to the bone.

Warnings

- The product must be used prior to the expiration date.
- For single use only.
- Do not re-sterilize.
- Do not use if packaging has been damaged and/or the product has been compromised. In the event packaging has been compromised, discard the product. Damaged packaging should be returned to the manufacturer.
- Do not use to support reduction of a defect site. Rigid fixation techniques are recommended as needed to assure stabilization of the defect in all planes. Screws must gain purchase in the host bone as opposed to the OsteoSurge 100.
- Do not use to repair bone defects where soft tissue coverage cannot be achieved as complete post-operative wound closure is necessary.
- Do not overfill the graft site.

Precautions

- OsteoSurge 100 is sterile for the duration of the product's shelf life, provided that the package is in its original sealed condition and that it is unopened and undamaged.
- As with all biological products, the tissue in OsteoSurge 100 has the potential to transmit infectious agents despite processing treatments, extensive donor screening, tissue selection and laboratory testing. To date, there have been no reports of experimental or clinical viral seroconversion attributed to the use of demineralized bone.
- As with any surgical procedure, the possibility of infection exists.
- Although the production technique is designed to eliminate antigenic properties of the product, the possibility of such a reaction is present.

OsteoSurge® 100 Demineralized Bone Matrix

Reference	Description	Size
56300010	Putty (syringe)	1cc
56300025	Putty (syringe)	2.5cc
56300050	Putty (syringe)	5cc
56300100	Putty (syringe)	10cc

- Once the container seal has been compromised, the tissue product shall be either transplanted, if appropriate, or otherwise discarded.
- Use caution with filling a closed defect. Resistance during extrusion may be an indication of over pressurization. Excessive pressurization of the device could result in fat embolization and/or embolization of the material into the bloodstream.
- When introducing OsteoSurge 100, care must be taken to avoid excessive compaction.
- Appropriate placement and/or fixation are critical factors in the avoidance of potentially adverse effects.
- Overfilling the implantation site should be avoided to achieve a tension-free closure of the wound.

* U.S. Patent Nos. 7,132,110; 7,811,608

1. Khaliq S, Lollis R, Bell D, Oliver R, Walsh WR, and Ingram R, Evaluation of a Next Generation DBM Putty in a Posterlateral Spinal Fusion Model, (2009) Integra LifeSciences Corporation.
2. Data on file
3. Chnari, E; Javoroncov, M; Gertzman AA; Sunwoo MH; Dunn, MG, Bone Morphogenetic Protein 2 (BMP-2) Levels are Predictive of the Osteoinductive Potential of Demineralized Bone. Matrix, 56th Annual Meeting of the Orthopaedic Research Society Poster No. 485.

SeaSpine

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Made in the U.S.A.

SeaSpine

OsteoSurge® 100

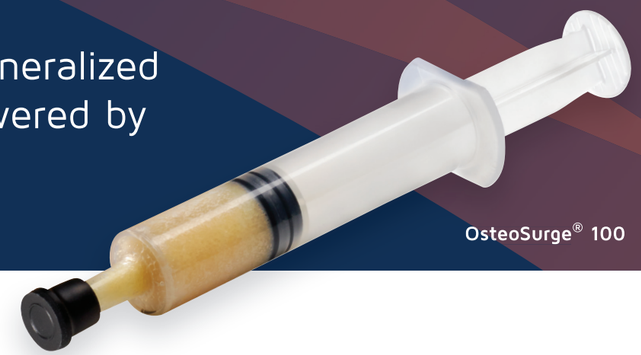
Demineralized Bone Matrix

OsteoSurge® 100

OsteoSurge® 100

SeaSpine's patented* Accell® process converts particulate DBM into a dispersed form, which offers early accessibility to naturally occurring inductive bone proteins.[1]

An Advanced Demineralized Bone Matrix — Powered by Accell® Technology



FEATURES

Accell® Bone Matrix

This patented, dispersed form of DBM offers significantly increased surface area, which provides access to the naturally occurring bone proteins contained in DBM.

Superior Handling

OsteoSurge 100 incorporates a poloxamer Reverse Phase Medium (RPM), a biocompatible carrier. This thermoreversible carrier allows OsteoSurge 100 to meet the needs of challenging surgical applications where robust handling is essential.

- At room temperature, OsteoSurge 100 is malleable and easily extruded from the syringe.
- At body temperature, OsteoSurge 100 is more viscous, resists irrigation and minimizes graft migration.

SeaSpine DBM: An Expert Approach to DBM Processing

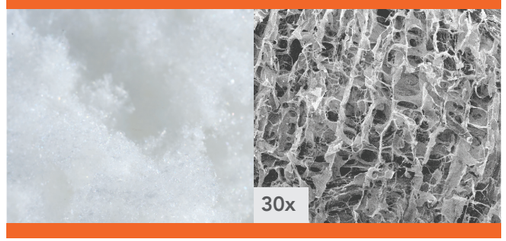
SeaSpine controls the processing of DBM and ABM from start to finish in its state-of-the-art facility. Each lot is tested in a validated *in vitro* assay to verify osteoinductive potential.[2]

Safety Through E-Beam Sterilization

SeaSpine utilizes electron beam (e-beam) sterilization to ensure product sterility. SeaSpine's sterilization process has not been shown to impact the osteoinductive potential of DBM.[2] All products are e-beam sterilized as the last step in manufacturing prior to being shipped.

The Accell® Advantage

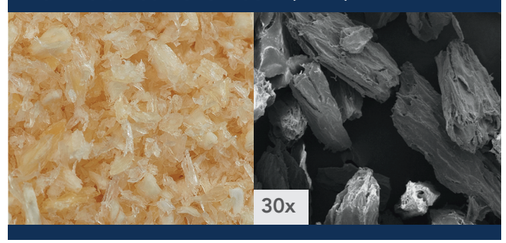
Accell Bone Matrix (ABM)



Open structure, dispersed DBM

- Transformed from particulate DBM
- Highly porous matrix with greater surface area
- Greater exposure to bone proteins compared to DBM

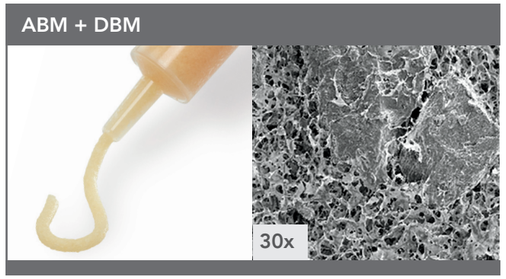
Demineralized Bone Matrix (DBM)



Standard, particulate DBM

- Formed by removing mineral component of cortical bone
- Dense matrix of Type-1 collagen
- Gradual access to naturally occurring bone proteins

ABM + DBM



The combination of ABM and particulate DBM provides for both immediate and sustained accessibility to naturally occurring bone proteins which are important for osteogenesis.[1]

SeaSpine's Patented Accell Bone Matrix

The process of demineralization retains the naturally osteoinductive elements in bone. These osteoinductive elements, including BMPs, play a critical role in the bone forming process. SeaSpine manufactures both standard DBM and a proprietary dispersed form of DBM, known as ABM which has also been shown to exhibit osteoinductive potential.